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=> d his

     (FILE 'HOME' ENTERED AT 13:33:08 ON 18 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
L1        153512 S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2         55988 S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3           423 S L1 AND L2
L4          1137 S POLYLACTIDE(3W)GLYCOLIDE?
L5             2 S L3 AND L4
L6           220 S L1 AND GLYCOLID?
L7            40 S L2 AND L6
L8            35 DUP REM L7 (5 DUPLICATES REMOVED)
                 E BERNSTEIN H/AU
L9           772 S E3
                 E ZHANG Y/AU
L10        29875 S E3
                 E KHAN M A/AU
L11         7371 S E3
                 E TRACY M A/AU
L12           52 S E3
L13        38042 S L9 OR L10 OR L11 OR L12
L14           11 S L6 AND L13
L15            5 DUP REM L14 (6 DUPLICATES REMOVED)
L16            3 S (ZINC (W)(CARBONAT? OR ACETAT? OR CHLORID? OR SULFATE? OR CIT
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NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
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NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 24	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

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FILE 'HCAPLUS' ENTERED AT 13:33:39 ON 18 OCT 2007
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FILE 'LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
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=> s (polymer? or matrix or gel or pellet? or particle?) and zinc
L1      153512 (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC

=> s (controlled or modulat?)(w)release?
L2       55988 (CONTROLLED OR MODULAT?)(W) RELEASE?

=> s l1 and l2
L3         423 L1 AND L2

=> s poly(lactide(3w)glycolide)?
MISSING OPERATOR 'POLY(LACTIDE'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s polylactide(3w)glycolide?
L4        1137 POLYLACTIDE(3W) GLYCOLIDE?

=> s l3 and l4
L5           2 L3 AND L4

=> d 1-2 ibib ab

L5   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:729499  HCAPLUS
DOCUMENT NUMBER:          143:199860
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TITLE: Composite materials for controlled release of water soluble products

INVENTOR(S): Yong, Tseh-Hwan; Ying, Jackie Y.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072125	A2	20050811	WO 2005-US1108	20050113
WO 2005072125	A3	20061102		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006024377	A1	20060202	US 2005-34217	20050113
US 7211275	B2	20070501		

PRIORITY APPLN. INFO.: US 2004-536710P P 20040116

AB Composite materials comprising a water-soluble compound adsorbed onto a basic inorg. material and a bio-degradable polymer which yields acidic degradation products, methods of producing same, and methods of use thereof are described, wherein the composite materials are designed so as to provide controlled release of the water soluble mol. Hydroxyapatite (I) prepared by chemical precipitation having average particle size 5.3 μm. I had high protein adsorbing capability and adsorbed 99.2% of FITC-BSA. Release of FITC-BSA from hydroxyapatite at various pH was studied.

L5 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:762783 HCAPLUS

DOCUMENT NUMBER: 135:322723

TITLE: Proteins deposited onto sparingly soluble biocompatible particles for controlled protein release into a biological environment from a polymer matrix

INVENTOR(S): Shih, Chung; Zentner, Gaylen; Piao, Ai-Zhi

PATENT ASSIGNEE(S): Macromed, Inc., USA

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076558	A1	20011018	WO 2001-US11217	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				

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            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2002015737          A1    20020207    US 2001-827100          20010405
     US 6998137             B2    20060214
     CA 2405030             A1    20011018    CA 2001-2405030         20010406
     EP 1267838             A1    20030102    EP 2001-924765          20010406
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     BR 2001010319          A     20030729    BR 2001-10319           20010406
     NZ 521994              A     20030829    NZ 2001-521994          20010406
     JP 2004507450          T     20040311    JP 2001-574076          20010406
     MX 2002PA09790         A     20030619    MX 2002-PA9790          20021004
     ZA 2002008039          A     20040204    ZA 2002-8039            20021007
     IN 2002MN01387         A     20040904    IN 2002-MN1387          20021007
PRIORITY APPLN. INFO.:                         US 2000-195700P      P  20000407
                                               US 2001-827100       A  20010405
                                               WO 2001-US11217      W  20010406
```

AB The present invention relates to compns. and methods for the modulated release of one or more proteins or peptides. The composition is comprised of a biocompatible polymeric matrix, a protein and/or peptide, and a sparingly water-soluble or essentially insol. particle. The protein is deposited by adsorption or some other mechanism onto the sparingly water-soluble biocompatible particle wherein the protein-particle combination is dispersed within the polymeric matrix. The deposition of the protein onto the particle acts to modulate the release of the protein or peptide from dosage forms including long-acting dosage systems. To a solution of 5 mg/3mL human growth hormone was added to 100 mg of zinc carbonate and the suspension was allowed to stand in a refrigerator at 4° for 16 h. HPLC anal. showed that the mass balance recovery of hGH, after removal of zinc using EDTA, was quant. In vivo pharmacokinetics of hGH sustained-release formulation was studied in rats.

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REFERENCE COUNT:          2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
L1        153512 S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2         55988 S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3           423 S L1 AND L2
L4          1137 S POLYLACTIDE(3W)GLYCOLIDE?
L5             2 S L3 AND L4

=> s l1 and glycolid?
L6           220 L1 AND GLYCOLID?

=> s l2 and l6
L7            40 L2 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            35 DUP REM L7 (5 DUPLICATES REMOVED)

=> d 1-35 ibib ab

L8   ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:817751  HCAPLUS
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DOCUMENT NUMBER: 147:197371
TITLE: Pharmaceutical compositions with enhanced stability for sustained controlled-release delivery, comprizing a salt of a peptide drug with a strong acid, biodegradable polymer, and release rate modifying excipients
INVENTOR(S): Li, Yuhua
PATENT ASSIGNEE(S): Quest Pharmaceutical Services, USA
SOURCE: PCT Int. Appl., 68pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007084460	A2	20070726	WO 2007-US1039	20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007196416	A1	20070823	US 2007-653636	20070116
PRIORITY APPLN. INFO.:			US 2006-759891P P	20060118

AB The present invention provides for a stabilized biodegradable polymeric composition useful as a controlled release delivery system for peptide agents. The compns. of the present invention comprise (a) a beneficial salt of a peptide agent formed with a strong acid that minimizes or prevents the interaction/reaction between the peptide agent and the polymer in an organic solution; (b) a biodegradable polymer; (c) a pharmaceutically acceptable organic solvent; and (d) optionally one or more excipients. The present invention also relates to a method of manufacturing and a method of use thereof. Thus, leuprolide hydrochloride was prepared from leuprolide acetate by replacing acetic acid with HCl through an ion-exchange and lyophilization procedure. Injectable composition was prepared with 106 mg leuprolide hydrochloride and 940 mg poly(DL-lactide-co-glycolide). At 4°, up to 23% of leuprolide was degraded in the polymeric composition containing leuprolide acetate, while less than 2% of leuprolide was degraded for those formulations containing leuprolide hydrochloride after 18 mo.

L8 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:561106 HCAPLUS
DOCUMENT NUMBER: 146:528408
TITLE: Progenitor endothelial cell capturing with a drug eluting implantable medical device
INVENTOR(S): Cottone, Robert John, Jr.; Rowland, Steven M.; Parker, Sherry; Yoklavich, Meg; Kutryk, Michael John Bradley
PATENT ASSIGNEE(S): Orbusneich Medical, Inc., USA
SOURCE: PCT Int. Appl., 87pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007059253	A2	20070524	WO 2006-US44423	20061115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2005-736920P	P	20051115
	US 2006-822451P	P	20060815
	US 2006-822465P	P	20060815
	US 2006-822471P	P	20060815

AB A medical device for implantation into vessels or luminal structures within the body is provided, which stimulates pos. blood vessel remodeling. The medical device, such as a stent and a synthetic graft, is coated with a pharmaceutical composition consisting of a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises a ligand such as a peptide, an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis. Thus, stents were coated with 500 μg of a coating composition containing 4% paclitaxel and 96% of a 50:50 poly(DL-lactide-co-glycolide) and incubated in 3 mL of bovine serum at 37° for 21 days. Paclitaxel released into the serum was measured using standard techniques at various days during the incubation period. The elution profile of paclitaxel release was very slow and controlled since only about 4 μg of paclitaxel were released from the stent in the 21-day period.

L8 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2007:352069 HCAPLUS
DOCUMENT NUMBER:	146:365740
TITLE:	Controlled release formulations containing duloxetine and solubilizers and polymer enteric coating
INVENTOR(S):	Prasad, Rudresha Korlakunte Virupakshaiah; Desomayanandam, Prabhakaran
PATENT ASSIGNEE(S):	Cadila Healthcare Limited, India
SOURCE:	PCT Int. Appl., 29pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007034503	A2	20070329	WO 2006-IN209	20060620
WO 2007034503	A3	20070712		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

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US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

IN 2005MU00718	A	20070629	IN 2005-MU718		20050620
PRIORITY APPLN. INFO.:			IN 2005-MU718	A	20050620

AB The preset invention provides a controlled release dosage form of duloxetine comprising a homogeneous core comprised of duloxetine or its pharmaceutically acceptable salts, pharmaceutically acceptable polymeric carrier, solubility enhancer, a hydrophobic component, a hydrodynamic diffusion enhancer, a viscolyzing agent and pharmaceutically acceptable excipients; a entering coat on said core and a barrier layer between said core and the enteric coat. For example, controlled release tablets contained duloxetine hydrochloride, HPMC, lactose, Xanthan gum, sodium alginate, and coatings of Eudragit L 100-55, tri-Et citrate.

L8 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:944242 HCAPLUS
DOCUMENT NUMBER: 147:243429
TITLE: Depot compositions with multiple drug release rate controls
INVENTOR(S): Chen, Guohua; Kleiner, Lothar Walter; Houston, Paul R.; Wright, Jeremy Corwin
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28pp., Cont.-in-part of U.S. Ser. No. 295,527.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2007196415	A1	20070823	US 2006-553925		20061027
US 2003170289	A1	20030911	US 2002-295527		20021114
PRIORITY APPLN. INFO.:			US 2002-295527	A2	20021114
			US 2001-336307P	P	20011114

AB Injectable depot compns. with dual mechanisms of release rate control are provided for sustained beneficial agent delivery in a patient. The composition includes bioerodible particles and an injectable depot vehicle containing a bioerodible polymer in an organic solvent, for forming a bioerodible depot implant after administration to the patient. The bioerodible particles are dispersed in the depot vehicle and contain a beneficial agent and a release rate controlling agent retarding the release of the beneficial agent from the bioerodible particles and from the depot implant. Depot gel vehicles comprising glycolide-lactide copolymer were prepared and various drug solns. such as HGH were loaded in the depot gel.

L8 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:594040 HCAPLUS
DOCUMENT NUMBER: 147:16687
TITLE: Progenitor endothelial cell capturing with a drug eluting implantable medical device
INVENTOR(S): Cottone, Robert John, Jr.; Yoklavich, Margaret; Parker, Sherry
PATENT ASSIGNEE(S): Orbusneich Medical, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S.

Ser. No. 76,131.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007123977	A1	20070531	US 2006-560353	20061115
WO 2003099169	A1	20031204	WO 2003-US15811	20030520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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US 2004039441	A1	20040226	US 2003-442669	20030520
CN 1655738	A	20050817	CN 2003-811531	20030520
JP 2005525911	T	20050902	JP 2004-506697	20030520
US 2007134290	A1	20070614	US 2006-494801	20060726

PRIORITY APPLN. INFO.:

US 2002-382095P	P	20020520
US 2003-442669	B2	20030520
US 2005-76131	A2	20050309
US 2005-736920P	P	20051115
US 2006-822465P	P	20060815
WO 2003-US15811	W	20030520

AB A medical device for implantation into vessels or luminal structures within the body is provided, which stimulates pos. blood vessel remodeling. The medical device, such as a stent and a synthetic graft, is provided with a coating with a pharmaceutical composition containing a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises one or more barrier layers, and a ligand such as a peptide, an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis.

L8 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:720149 HCAPLUS
DOCUMENT NUMBER: 147:219561
TITLE: Design and Development of a Novel Controlled Release PLGA Alginate-Pectinate Polyspheric Drug Delivery System
AUTHOR(S): Sweet, Joe L.; Pillay, Viness; Choonara, Yahya E.
CORPORATE SOURCE: Webster Surgical Center, Tallahassee, FL, USA
SOURCE: Drug Delivery (2007), 14(5), 309-318
CODEN: DDELEB; ISSN: 1071-7544
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A 23 full factorial design was employed to evaluate and optimize the drug entrapment efficiency and in vitro drug release from PLGA microparticles encapsulated in a complex crosslinked alginate-pectinate matrix (polysphere). The independent formulation variables included the volume of internal and external phases, and concentration of PLGA. Surface morphol. and internal structure of PLGA microparticles and polyspheres were examined by

SEM which revealed spherical PLGA microparticles with highly porous surfaces that accounted for the rapid burst effect of this system. Texture anal. was used to profile the matrix resilience, tolerance, and energy absorbed. In vitro drug release was assessed in buffer media on PLGA microparticles and polyspheres. Polyspheres exhibited ideal zero-order release while PLGA microparticles had a burst effect followed by lag phase. Kinetic modeling of in vitro drug release data indicated that formulations were not highly dependent on polymeric erosion as a mechanism for drug release but rather diffusion. A close correlation existed between the matrix tolerance and energy absorbed. Formulations with decreased tolerance absorbed less energy, thus led to rapid surface erosion, lower matrix integrity and hence a burst effect. The converse was true for an increased matrix tolerance, which led to zero-order release supported by superior matrix integrity and a significantly reduced burst effect. The rat s.c. model validated in vitro release data and demonstrated that the polyspheres provided flexible yet superior rate-modulated drug delivery.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1249147 HCAPLUS
DOCUMENT NUMBER: 146:13196
TITLE: Cores of a polymer and a drug and microcapsules suitable for parenteral administration as well as process for their manufacture
INVENTOR(S): Gustafsson, Nils Ove; Joensson, Monica; Laakso, Timo
PATENT ASSIGNEE(S): Stratosphere Pharma AB, Swed.
SOURCE: Eur. Pat. Appl., 23pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1726299	A2	20061129	EP 2005-28165	20051222
EP 1726299	A3	20070418		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
WO 2006125620	A2	20061130	WO 2006-EP4940	20060524
WO 2006125620	A3	20070802		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRIORITY APPLN. INFO.: EP 2005-11516 A 20050527
EP 2005-28165 A 20051222

AB The present invention relates to novel processes for the manufacture of cores of a specific polymer, e.g., polyarginine, amylopectin, dextran hyaluronic acid, Na CM-cellulose, etc., and a biol. active substance, and of such cores carrying a shell, i.e. microcapsules, to the cores and microcapsules thus produced, and to a pharmaceutical composition comprising

such microcapsules. Thus, human growth hormone (GH) was lyophilized in the presence of ammonium acetate then suspended in isopropanol and allowed to air dry. Maltodextrin (mol. weight <3.5 kDa, 5 g) was also lyophilized. Maltodextrin microspheres in which the GH was suspended manually were prepared, mixed with Miglyol 829, homogenized, left under refrigeration over night, centrifuged, washed, allowed to air dry and sieved. The 38 to 125 μm fraction had a loading of 11% and the 125 to 180 μm fraction 18%, which corresponds to 53% and 90% of the target core load, resp. The dimer content was approx. 3%, compared to about 2.4% in the starting material, and no polymer forms were detected. The fractions were pooled to provide about 0.57 g of cores.

L8 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:90179 HCAPLUS
DOCUMENT NUMBER: 147:31493
TITLE: Synthesis of polymeric biocompatible materials for controlled drug delivery by means of supercritical technology
AUTHOR(S): Rodriguez, Juan Francisco; de Lucas, Antonio; Gracia, Ignacio; Mazarro, Rosario
CORPORATE SOURCE: Department of Chemical Engineering. Faculty of Chemistry, University of Castilla-La Mancha, Ciudad Real, 13004, Spain
SOURCE: Medical Polymers 2006, [International Conference Focusing on Polymers Used in the Medical Industry], 5th, Cologne, Germany, June 6-7, 2006 (2006), 22/1-22/8. Rapra Technology Ltd.: Shrewsbury, UK. CODEN: 69IVF9; ISBN: 1-85957-580-3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The objective of the project is the development of a new technique based on supercrit. technol. for the production of bioadsorbable polymeric microparticles containing pharmaceutical principles, for their use in the controlled release of medicines. For this purpose we studied the ring-opening copolymn. of D,L-lactide and glycolide in supercrit. carbon dioxide using zinc (II) 2-ethylhexanoate (ZnOct2) as catalyst. Expts. were performed at various reaction times (from 1 to 18 h), pressures (from 150 to 250 bar) and stirring rates (from 50 to 2200 rpm). Gel permeation chromatog. (GPC) and DTA were used to determine polymers mol. wts. distribution and conversion, resp.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:729499 HCAPLUS
DOCUMENT NUMBER: 143:199860
TITLE: Composite materials for controlled release of water soluble products
INVENTOR(S): Yong, Tseh-Hwan; Ying, Jackie Y.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072125	A2	20050811	WO 2005-US1108	20050113
WO 2005072125	A3	20061102		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

US 2006024377	A1	20060202	US 2005-34217	20050113
US 7211275	B2	20070501		
PRIORITY APPLN. INFO.:			US 2004-536710P	P 20040116

AB Composite materials comprising a water-soluble compound adsorbed onto a basic inorg. material and a bio-degradable polymer which yields acidic degradation products, methods of producing same, and methods of use thereof are described, wherein the composite materials are designed so as to provide controlled release of the water soluble mol. Hydroxyapatite (I) prepared by chemical precipitation having average particle size 5.3 μm. I had high protein adsorbing capability and adsorbed 99.2% of FITC-BSA. Release of FITC-BSA from hydroxyapatite at various pH was studied.

L8 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:823153 HCAPLUS
DOCUMENT NUMBER: 143:210893
TITLE: Compositions and methods for timed release of water-soluble nutritional supplements
INVENTOR(S): Romero, Jaime
PATENT ASSIGNEE(S): Colombia
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005181047	A1	20050818	US 2004-782245	20040218
US 2005181048	A1	20050818	US 2004-910787	20040803
US 2005181044	A1	20050818	US 2004-930560	20041209
WO 2005079764	A1	20050901	WO 2005-US4890	20050216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

BR 2005002357	A	20070221	BR 2005-2357	20050621
PRIORITY APPLN. INFO.:			US 2004-782245	A2 20040218
			US 2004-910787	A2 20040803

AB The present invention relates to compns. of and methods for producing timed or retarded release formulations that contain glucosamine sulfate, beta-(1,4)-2-amino-2-deoxy-D-glucose, and chondroitin, (C14H19NO14SNa2)n; N-acetylchondrosanine (2-acetamide-2-deoxy-D-galactopyranose) and D-guluronic acid copolymer and/or their dietary and nutraceutically acceptable salts of the same and/or hydrates of the active substance that provide a timed release formulation of the active substance.

L8 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:433684 HCAPLUS
DOCUMENT NUMBER: 140:429037
TITLE: High viscosity liquid controlled drug delivery system and medical or surgical device
INVENTOR(S): Gibson, John W.; Miller, Stacey S.; Middleton, John C.; Tipton, Arthur J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 699,002.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004101557	A1	20040527	US 2002-316441	20021210
US 5747058	A	19980505	US 1995-474337	19950607
EP 1525858	A1	20050427	EP 2005-75143	19960607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1781555	A	20060607	CN 2005-10104020	19960607
US 6413536	B1	20020702	US 1999-385107	19990827
US 7053209	B1	20060530	US 2000-699002	20001026
AU 2003200423	A1	20030410	AU 2003-200423	20030207
WO 2004052336	A2	20040624	WO 2003-US39311	20031210
WO 2004052336	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003297848	A1	20040630	AU 2003-297848	20031210
AU 2006203112	A1	20060810	AU 2006-203112	20060720
JP 2007126459	A	20070524	JP 2006-304264	20061109

PRIORITY APPLN. INFO.:

US 1995-474337	A2	19950607
US 1995-478450	B2	19950607
US 1997-944022	A2	19970915
US 1999-385107	A3	19990827
US 2000-699002	A2	20001026
CN 1996-195895	A3	19960607
EP 1996-921521	A3	19960607
JP 1997-502181	A3	19960607
AU 1998-94750	A3	19980908
US 2002-316441	A	20021210
AU 2003-200423	A3	20030207
WO 2003-US39311	W	20031210

AB The present invention relates to novel nonpolymeric compds. and compns. that form liquid, high viscosity materials suitable for the delivery of biol. active substances in a controlled fashion, and for use as medical or surgical devices. The materials can optionally be diluted with a solvent to form a material of lower viscosity, rendering the material easy to administer. This solvent may be water insol. or water soluble, where the water soluble solvent rapidly diffuses or migrates away from the material in vivo, leaving a higher viscosity liquid material. 1,6-Hexanediol lactate ε-hydroxycaproic acid produced in was dissolved in N-methylpyrrolidone at a weight ratio of 70:30. Bupivacaine base (10%) was

then added to this mixture Drops weighing approx. 100 mg were precipitated into 40
mL buffer. At 4 h, around 4.1 weight% of the bupivacaine contained in the precipitated drop had been released. At 24 h, around 8.6 weight% of the bupivacaine
had been released.

L8 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:310636 HCAPLUS
DOCUMENT NUMBER: 140:327079
TITLE: Polymer compositions for stabilization and controlled release of formaldehyde-treated vaccine antigens
INVENTOR(S): Schwendeman, Steven P.; Jiang, Wenlei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Pat. Appl. 2002 9,493.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004071715	A1	20040415	US 2003-417841		20030417
US 2002009493	A1	20020124	US 2000-738961		20001215
US 6743446	B2	20040601			
PRIORITY APPLN. INFO.:			US 1999-170983P	P	19991215
			US 2000-738961	A2	20001215
			US 2002-373858P	P	20020419

AB A delivery system and a method for sustained release of formaldehyde-treated vaccine antigens wherein the antigens are stabilized by agents mixed with the formaldehyde-treated antigens and then dispersed within a biocompatible polymer matrix. The stabilizing agents inhibit formaldehyde mediated aggregation of formaldehyde-treated vaccine antigens by >60% compared to antigens incubated without stabilizing agents. Stabilizing agents may be selected from formaldehyde-interacting amino acids, basic additives, and mono-, di-, or polysaccharides. The delivery system may be biodegradable. The formaldehyde-treated vaccine antigens may be tetanus toxoid, diphtheria toxoid, or both tetanus toxoid and diphtheria toxoid. One-month continuous release of stable BSA from microspheres was achieved when PEG content in the PLA/PEG blends was above 20%. The blend of PEG with PLA appears to improve the microclimate, i.e., by avoiding the acidic microclimate and increasing the water content to stabilize BSA encapsulated in microspheres. The stabilization of BSA in the PLA/PEG microspheres may also be attributed in part to the increased water content in the formulation.

L8 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:561533 HCAPLUS
DOCUMENT NUMBER: 143:154203
TITLE: Biodegradable triblock polyester and its preparation
INVENTOR(S): Cao, Amin
PATENT ASSIGNEE(S): Shanghai Institute of Organic Chemistry, CAS, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1546549	A	20041117	CN 2003-10109099	20031204
PRIORITY APPLN. INFO.:			CN 2003-10109099	20031204

AB A biodegradable triblock polyester having a Mn of 1,000-300,000, which can be used for medical materials and control releasing drug delivery system, is prepared by polymn. of a diol and a diester at 120-300° and 1-5 + 104 Pa in the presence of a catalyst, such as sulfonic acid and tin tetrachloride, to receive a polyester macro-initiator, which is used to initiate the polymn. of a cyclolactone, such as glycolide and lactide. Thus, succinic acid and 1,4-butanediol were polymd. to receive a polyester, which was used as initiator for the polymn. of L,L-lactide in the presence of tin octoate to obtain a triblock polyester.

L8 ANSWER 14 OF 35 MEDLINE on STN

ACCESSION NUMBER: 2004280307 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15180341
TITLE: Control of blood glucose by novel GLP-1 delivery using biodegradable triblock copolymer of PLGA-PEG-PLGA in type 2 diabetic rats.
AUTHOR: Choi Suna; Baudys Miroslav; Kim Sung Wan
CORPORATE SOURCE: Center for Controlled Chemical Delivery (CCCD), Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, Utah 84112, USA.
SOURCE: Pharmaceutical research, (2004 May) Vol. 21, No. 5, pp. 827-31.
Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 8 Jun 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 7 Dec 2004

AB PURPOSE: The incretin hormone glucagon-like peptide-1 (GLP-1) is a promising candidate for treatment of type 2 diabetes mellitus. However, plasma half-life of GLP-1 is extremely short, thus multiple injections or continuous infusion is required for therapeutic use of GLP-1. Therefore, we investigated a new delivery system as a feasible approach to achieve sustained GLP-1 release for a 2-week period. METHODS: A water-soluble, biodegradable triblock copolymer of poly [(DL-lactide-co-glycolide)-b-ethylene glycol-b-(DL-lactide-coglycolide)] (ReGel) was used in this study as an injectable formulation for controlled release of GLP-1. GLP-1 was formulated into ReGel as insoluble zinc complex to stabilize GLP-1 against aggregation and slow down release. The GLP-1 release profile was monitored in vitro and in vivo. Zucker Diabetic Fatty rats were administered subcutaneously with the GLP-1 formulation. The concentration of GLP-1, insulin, and glucose was monitored every day after the GLP-1 administration. RESULTS: The GLP-1 release from ReGel formulation in vitro and in vivo showed no initial burst and constant release for 2 weeks. Animal study demonstrated that the plasma insulin level was increased, and the blood glucose level was controlled for 2 weeks by one injection of ReGel/ ZnGLP-1 formulation. CONCLUSIONS: It is concluded that one injection of zinc -complexed GLP-1 loaded ReGel can be used for delivery of bioactive GLP-1 during a 2-week period. Because this new delivery system is biocompatible and requires twice-a-month injection, it can improve patient compliance and cost-effectiveness.

L8 ANSWER 15 OF 35 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:202145 SCISEARCH
THE GENUINE ARTICLE: 774XU
TITLE: Biodegradable triblock copolymer microspheres based on thermosensitive sol-gel transition
AUTHOR: Kwon Y M; Kim S W (Reprint)
CORPORATE SOURCE: Univ Utah, Dept Pharmaceut & Pharmaceut Chem, Ctr Controlled Chem Delivery, Salt Lake City, UT 84112 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: PHARMACEUTICAL RESEARCH, (FEB 2004) Vol. 21, No. 2, pp. 339-343.
ISSN: 0724-8741.
PUBLISHER: KLUWER ACADEMIC/PLENUM PUBL, 233 SPRING ST, NEW YORK, NY 10013 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 21
ENTRY DATE: Entered STN: 5 Mar 2004
Last Updated on STN: 5 Mar 2004

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose. The purpose of this study is to design microspheres for sustained protein delivery using thermosensitive, biodegradable triblock copolymer, poly (D,L-lactide-co-glycolide)-b-poly (ethylene glycol)b- poly (D, L-lactide-co-glycolide) (PLGA-PEG-PLGA) without using organic solvent.

Methods. Microspheres of the triblock copolymer PLGA- PEG-PLGA were prepared in an aqueous-based method without using methylene chloride (Msp A). This method used the sol - gel transition property of the polymer. The size and morphology of the microspheres were examined by optical microscopy and scanning electron microscopy (SEM). Zinc crystalline recombinant human insulin was incorporated in Msp A as well as in the microspheres of the same polymer prepared by the conventional water-in-oil-in-water (w/o/w) double emulsion method using methylene chloride (Msp B). Insulin release from both microspheres was carried out using high-performance liquid chromatography (HPLC) as well as circular dichroism (CD) spectroscopy of released insulin. FITC-insulin-loaded Msp A and Msp B were observed under confocal microscopy. Both microspheres were injected subcutaneously to SD rats with diabetes induced by streptozotocin. Blood glucose and plasma insulin levels were monitored.

Results. Although the insulin release from Msp B exhibited initial burst and incomplete release, Msp A showed significant reduction of initial burst and continuous release over 3 weeks (> 85%). CD spectra of released insulin showed that insulin from Msp A preserved its secondary structural integrity, whereas that from Msp B indicated changes in conformation. Confocal microscopy of FITC-insulin-loaded microspheres (both A and B) showed that the observed release profile may be attributed to homogeneous distribution of FITC-insulin within Msp A but inhomogeneiety in Msp B. Both microspheres were injected s.c. to diabetic rats. Whereas Msp B caused a burst effect (hypoglycemia) followed by quick change in blood glucose and insulin level, Msp A exhibited relatively sustained release of insulin and blood glucose level for at least 10 days.

Conclusions. The PLGA- PEG-PLGA microspheres (Msp A) demonstrated continuous release of insulin in vitro and in vivo without serious burst effect and incomplete release, as shown by Msp B.

L8 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:2669 HCAPLUS
DOCUMENT NUMBER: 140:65193
TITLE: Resorbable matrixes with coatings for delivery of bioactive compounds
INVENTOR(S): Royer, Garfield P.
PATENT ASSIGNEE(S): Royer Biomedical, Inc., USA

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004000276	A1	20031231	WO 2003-US19006		20030617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003243607	A1	20040106	AU 2003-243607		20030617
US 2005266077	A1	20051201	US 2004-518035		20041214
PRIORITY APPLN. INFO.:			US 2002-389933P	P	20020620
			WO 2003-US19006	W	20030617

AB This invention relates to the production and use of coated inorg.-biopolymer complexes for the controlled release of bioactive compds. including medicinals. Advantageously, the delivery system compns. include an inorg. such as calcium sulfate, a matrix polymer, and a coating. Matrix-azoalbumin microgranules were coated with HPMC.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:855782 HCAPLUS
DOCUMENT NUMBER: 139:341774
TITLE: Polymer compositions stabilization and control the release of formaldehyde-treated vaccine antigens
INVENTOR(S): Schwendeman, Steven P.; Jiang, Wenlei
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003088946	A1	20031030	WO 2003-US12032		20030418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003225057	A1	20031103	AU 2003-225057		20030418
PRIORITY APPLN. INFO.:			US 2002-373858P	P	20020419
			WO 2003-US12032	W	20030418

AB A delivery system and a method for sustained release of formaldehyde-treated vaccine antigens wherein the antigens are stabilized by stabilizing agents mixed with the formaldehyde-treated antigens and then dispersed within a biocompatible polymer matrix is disclosed. The stabilizing agents inhibit formaldehyde mediated aggregation of formaldehyde-treated vaccine antigens by >60% compared to antigens incubated without stabilizing agents. Stabilizing agents may be selected from formaldehyde-interacting amino acids, basic additives, and mono-, di-, or polysaccharides. The delivery system may be biodegradable. The formaldehyde-treated vaccine antigens may be tetanus toxoid, diphtheria toxoid, or both tetanus toxoid and diphtheria toxoid. Formaldehyde, with no stabilizing agents added, the antigenicity of tetanus toxoid was decreased to 28%. The toxoid with histidine and lysine and sorbitol retained above 80% antigenicity after 22 days of incubation.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:390755 HCAPLUS
DOCUMENT NUMBER: 138:364205
TITLE: Animal repellent controlled release compositions containing plant-derived alkaloids
INVENTOR(S): O'Leary, Robert K.
PATENT ASSIGNEE(S): The Corato Foundation, USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6565867	B1	20030520	US 2000-735071	20001212
US 2003202998	A1	20031030	US 2003-419882	20030422
US 6926901	B2	20050809		
US 2004151750	A1	20040805	US 2004-758123	20040116
US 7052708	B2	20060530		

PRIORITY APPLN. INFO.: US 2000-735071 A2 20001212
US 2003-419882 A2 20030422

AB Animal repellent composition combination comprises a plant bulb, and one or more plant derived, animal repellent chems., such as one or more alkaloids isolated from one or more members of the family Amaryllidaceae and the family Liliaceae, preferably from one or more members of the genus Narcissus, and one or more polymers selected from the group consisting of a biodegradable polymer, an absorbable polymer, and a controlled release polymer, wherein the polymers form a matrix with the plant derived, animal repellent chems. to permit sustained release of the chems. The animal repellent composition of the invention may further contain permeation enhancers, plant nutrients, fertilizers, and plant rooting hormones.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 35 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 1
ACCESSION NUMBER: 2003:285752 SCISEARCH
THE GENUINE ARTICLE: BW36V
TITLE: Controlled drug delivery from injectable biodegradable triblock copolymer
AUTHOR: Kim Y J (Reprint); Kim S W
CORPORATE SOURCE: Univ Utah, Ctr Controlled Chem Delivery, 30 So 2000 E, Room 201, Salt Lake City, UT 84112 USA (Reprint); Univ

Utah, Ctr Controlled Chem Delivery, Salt Lake City, UT 84112 USA
COUNTRY OF AUTHOR: USA
SOURCE: POLYMER GELS: FUNDAMENTALS AND APPLICATIONS, (2003) Vol. 833, pp. 300-311.
ISSN: 0097-6156.
PUBLISHER: AMER CHEMICAL SOC, 1155 SIXTEENTH ST NW, WASHINGTON, DC 20036 USA.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ENTRY DATE: Entered STN: 11 Apr 2003
Last Updated on STN: 11 Apr 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ABA and BAB triblock copolymers composed of poly(DL-lactide-co-glycolide) (PLGA) and poly(ethylene glycol) (PEG) were used in this study. It is a new biodegradable and injectable implant system, which has sol to gel transition behavior. It is a sol between 5 and 30 degreesC but forms a gel at the body temperature in an aqueous solution. Two model drugs, ketoprofen and spironolactone, which have different hydrophobicities, were released from the PEG-PLGA-PEG triblock copolymer hydrogel. Ketoprofen was released over 2 weeks while spironolactone was released over more than 2 months with a sigmoid release profile. Human insulin was released from the PLGA-PEG-PLGA triblock copolymer hydrogel in a sink condition of phosphate buffer saline solution. We tried to modify the association states of insulin by zinc in order to inhibit the initial burst effect and obtain a constant release rate. Insulin associated from monomer and dimer to hexamer with increasing zinc concentration. The insulin release profile showed the constant release rate over more than 2 weeks. (C) 2003 American Chemical Society.

L8 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:716020 HCAPLUS
DOCUMENT NUMBER: 137:253053
TITLE: Medical devices and compositions for treating vulnerable plaque
INVENTOR(S): Brown, David L.
PATENT ASSIGNEE(S): Volcano Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002072014	A2	20020919	WO 2002-US7244		20020308
WO 2002072014	A3	20030424			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002254158	A1	20020924	AU 2002-254158		20020308
US 2003004141	A1	20030102	US 2002-96131		20020308
PRIORITY APPLN. INFO.:			US 2001-274331P	P	20010308
			WO 2002-US7244	W	20020308

AB Medical devices, compns. and methods for treating or preventing atherosclerotic plaque rupture are disclosed. Specifically, medical devices that deliver to a treatment site metalloproteinase inhibitors (MMPI) are disclosed. The medical devices include catheters, guide wires, vascular stents, micro-particles, electronic leads, probes, sensors, drug depots, transdermal patches, and vascular patches. Representative MMPIs included zinc chelators, urea derivs., caprolactone-based inhibitors, phosphonamides, piperazines, sulfonamides, tertiary amines, carbamate derivs., mercapto alcs., mercapto ketones, antimicrobial tertracyclines, non-antimicrobial tetracyclines, and derivs. and combinations thereof. In one embodiment a self-expanding vascular stent is coated with at least one MMPI and deployed at a site within an artery where vulnerable plaque has been identified.

L8 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:466547 HCAPLUS
DOCUMENT NUMBER: 137:37682
TITLE: Bioactive agent delivering system comprised of microparticles within a biodegradable to improve release profiles
INVENTOR(S): Shih, Chung; Zenter, Gaylen
PATENT ASSIGNEE(S): Macromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 559,507.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002076441	A1	20020620	US 2001-906041	20010713
US 6589549	B2	20030708		
US 6287588	B1	20010911	US 2000-559507	20000427
CA 2453507	A1	20030123	CA 2002-2453507	20020712
WO 2003005961	A2	20030123	WO 2002-US22017	20020712
WO 2003005961	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002320441	A1	20030129	AU 2002-320441	20020712
EP 1414406	A2	20040506	EP 2002-749958	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1527698	A	20040908	CN 2002-814093	20020712
JP 2004536836	T	20041209	JP 2003-511770	20020712
PRIORITY APPLN. INFO.:			US 2000-559507	A2 20000427
			US 1999-131562P	P 19990429
			US 2001-906041	A 20010713
			WO 2002-US22017	W 20020712

AB A composition and method for releasing a bio-active agent or a drug within a biol. environment in a controlled manner is disclosed. The composition is a dual phase polymeric agent-delivery composition comprising a continuous biocompatible gel phase, a discontinuous particulate phase comprising defined microparticles and an agent to be delivered. A microparticle containing a bio-active agent is releasably entrained within a

biocompatible polymeric gel matrix. The bioactive agent release may be contained in the microparticle phase alone or in both the microparticles and the gel matrix. The release of the agent is prolonged over a period of time, and the delivery may be modulated and/or controlled. In addition, a second agent may be loaded in some of the microparticles and/or the gel matrix. A microparticle reverse thermal gelation agent delivery system contained Zn-hGH incorporated into glycolide-lactide copolymer microspheres.

L8 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:72718 HCAPLUS
DOCUMENT NUMBER: 136:123690
TITLE: Methods for stabilizing drugs encapsulated in biodegradable controlled-release polymers
INVENTOR(S): Schwendeman, Steven P.; Zhu, Gaozhong; Bentz, Hanne; Hubbell, Jeffrey A.; Jiang, Wenlei; Shenderova, Anna; Kang, Jichao
PATENT ASSIGNEE(S): The Ohio State University Research Foundation, USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002009493	A1	20020124	US 2000-738961		20001215
US 6743446	B2	20040601			
US 2004071715	A1	20040415	US 2003-417841		20030417
US 2004105878	A1	20040603	US 2003-700107		20031103
PRIORITY APPLN. INFO.:			US 1999-170983P	P	19991215
			US 2000-738961	A2	20001215
			US 2002-373858P	P	20020419

AB Methods for reducing or inhibiting the irreversible inactivation of water-soluble drugs in biodegradable polymeric delivery systems which are designed to release such agents over a prolonged period of time, such as PLGA delivery systems are provided. The method comprises preparing a PLGA delivery systems whose microclimate, i.e., the pores where the active agent resides, uniformly or homogeneously maintain a pH of between 3 and 9, preferably between 4 and 8, more preferably between 5 and 7.5 during biodegrdn. Depending on the size of the delivery system, and the initial bulk permeability of the polymer, this result is achieved by (a) incorporating a water-soluble carrier into the delivery system, (b) incorporating a select basic additive (or antacid) into the delivery system, (c) incorporating both a water soluble carrier and a select basic additive into the delivery system, (d) adding a pore forming mol. for increasing the rate of release of low mol. weight monomers and oligomers into the delivery system, (e) using a PLGA polymer with reduced glycolide content, i.e. PLGA containing 100 to 75% lactide and 0 to 25% glycolide (f) using a microencapsulation method that yields a more extensive pore-network, e.g., oil-in-oil emulsion-solvent extraction as opposed to water-in-oil-in water-solvent evaporation method, and (g) combinations thereof. Tissue plasminogen activator (tPA) was successfully encapsulated into PLGA implants. Controlled release systems for local delivery was developed by using hydrogel to control wound healing. A multi-drug controlled release implant with tPA encapsulated was also tested for the intraocular management of proliferative vitroretinopathy. Here, 10% tPA powder was encapsulated as received (2% tPA, 75% arginine, 22% phosphoric acid, and 1% Polysorbate 80) with or without 3% Mg(OH)2 into PLGA milli-cylinders. Arginine-HCl and BSA were added in the release medium to improve the

stability of released tPA. With Mg(OH)2 encapsulated, the 1-mo release of tPA was increased from 77.1 to 98.0% and the recovery (released part + active residue) was increased from 82.7 to 100.1%, resp.

L8 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:31952 HCAPLUS
DOCUMENT NUMBER: 136:90989
TITLE: Controlled release microencapsulated formulations of nerve growth factor
INVENTOR(S): Cleland, Jeffrey L.; Lam, Xanthe M.; Duenas, Eileen T.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002004481	A1	20020110	US 1998-95911	19980611
US 6663899	B2	20031216		
US 2003203040	A1	20031030	US 2003-442894	20030520
US 7163701	B2	20070116		
PRIORITY APPLN. INFO.:			US 1997-49541P P	19970613
			US 1998-95911 A1	19980611

AB Nerve growth factor (NGF), particularly human recombinant NGF (rhNGF), is microencapsulated for controlled and sustained release. A method of making a microsphere having a decreased NGF aggregation characteristic and enhanced NGF stability comprises mixing NGF in solution with an NGF-stabilizing metal salt that binds NGF in a NGF/metal molar ratio of 1-4:1-50, and microencapsulating the NGF-metal mixture to form a microsphere capable of controlled sustained release of NGF. The metal is an alkali metal, alkaline earth metal, or polyvalent metal. The microencapsulation comprises drying the NGF-metal solution, dispersing a biodegradable polymer in an organic solvent, admixing the dried NGF mixture with the biodegradable polymer organic solvent mixture, spraying the NGF-biodegradable polymer mixture to form droplets, and removing the organic solvent from the droplets to form microspheres containing NGF. The microencapsulated formulations are used in promoting nerve cell growth, repair, survival, differentiation, maturation or function. For example, poly(lactide-co-glycolide) (PLGA) microspheres of rhNGF were prepared using zinc carbonate which greatly reduced the initial drug release. The PLGA microspheres provided a continuous release of rhNGF over 7 to 14 days. The zinc and rhNGF may form a stable complex that slowly dissocs. from the PLGA microspheres.

L8 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:130616 HCAPLUS
DOCUMENT NUMBER: 137:315871
TITLE: A novel sustained-release formulation of insulin with dramatic reduction in initial rapid release
AUTHOR(S): Takenaga, Mitsuko; Yamaguchi, Yoko; Kitagawa, Aki; Ogawa, Yasuaki; Mizushima, Yutaka; Igarashi, Rie
CORPORATE SOURCE: Institute of Medical Science, St. Marianna University School of Medicine, Miyamae-ku, Kawasaki, 216-8512, Japan
SOURCE: Journal of Controlled Release (2002), 79(1-3), 81-91
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To ensure a strictly controlled release of insulin, a preparation method for insulin-loaded microcapsules was designed.

Microcapsules were prepared with an injectable, biodegradable polymer composed of co-poly(d,l-lactic/glycolic) acids (PLGA) (mean mol. weight 6600, LA/GA ratio 50:50). Morphol. examination using scanning electron microphotog. demonstrated spherical particles with a main diameter of 15-30 μm. When 3% insulin-loaded PLGA microcapsules were administered s.c. as a single dose (250 U/kg) to streptozotocin-induced hyperglycemic rats, plasma insulin levels increased and were sustained at levels showing hypoglycemic effects. When glycerin, ethanol, or distilled water was used throughout the preparation procedure, the resultant microcapsules dramatically reduced the initial burst. The formulation in which glycerin was added to an oil phase containing PLGA, insulin, and ZnO increased plasma insulin levels to 86.7, 108.4, and 84.9 μU/mL at 1, 2, and 6 h, resp. The levels remained at 36.2-140.7 μU/mL from day 1 to day 9. The AUC0-24 h/AUC0-336 h ratio was calculated to be 9.7%. The formulation prepared without additives gave such a rapid insulin release that animals receiving it became transiently hypoglycemic.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:798097 HCAPLUS

DOCUMENT NUMBER: 135:348966

TITLE: Antimicrobial bioabsorbable polymeric materials

INVENTOR(S): Burrell, Robert Edward; Yin, Hua Qing; Djokic, Stojan; Langford, Rita Johannna Mary

PATENT ASSIGNEE(S): Westaim Biomedical Corp., Can.

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001080920	A2	20011101	WO 2001-CA498		20010417
WO 2001080920	A3	20020411			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 2001055622	A1	20011227	US 2001-835859		20010416
US 6719987	B2	20040413			
CA 2403441	A1	20011101	CA 2001-2403441		20010417
EP 1274473	A2	20030115	EP 2001-921078		20010417
EP 1274473	B1	20060705			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003530972	T	20031021	JP 2001-578014		20010417
AT 332156	T	20060715	AT 2001-921078		20010417
ES 2267746	T3	20070316	ES 2001-1921078		20010417
PRIORITY APPLN. INFO.:			US 2000-197959P	P	20000417
			WO 2001-CA498	W	20010417

AB The invention provides bioabsorbable materials with antimicrobial coatings or powders which provide an effective and sustainable antimicrobial effect. Specifically, this invention provides bioabsorbable materials comprising a bioabsorbable substrate associated with one or more

antimicrobial metals being in a crystalline form characterized by sufficient atomic disorder, such that the bioabsorbable material in contact with an alc. or water based electrolyte, releases atoms, ion, mols., or clusters of at least one antimicrobial metal at a concentration sufficient to provide an antimicrobial effect. The one or more antimicrobial metals do not interfere with the bioabsorption of the bioabsorbable material, and do not leave behind particulates lager than 2 μm, as measured 24 h after the bioabsorbable material has disappeared. Most preferably, the particulate sizing from the coating or powder is < 1 μm, as measured 24 h after the bioabsorbable material has disappeared. Particulates are thus sized to avoid deleterious immune responses or toxic effects. Such antimicrobial metals are in the form of a continuous or discontinuous coating, a powder, or a coating on a bioabsorbable powder. The antimicrobial coating is thin, preferably less than 900 nm or more preferably less than 500 nm, and very fine grained, with a grain size (crystallite size) of preferably less than 100 nm, more preferably less than 40 nm, and most preferably less than 20 nm. The antimicrobial coating is formed of an antimicrobial metal, which is overall crystalline, but which is created with atomic disorder, and preferably also having either or both of (a) a high oxygen content, as evidenced by a rest potential greater than about 225 mV, more preferably greater than about 250 mV, in 0.15 M Na2CO3 against a SCE (standard calomel electrode), or (b) discontinuity in the coating. The antimicrobial metal associated with the bioabsorbable substrate may also be in the form of a powder, having a particle size of less than 100 μ, or preferably less than 40 μm, and with a grain size (crystallite size) of preferably less than 100 μm, more preferably less than 40 nm, and most preferably less than 20 nm. Such powders may be prepared as a coating preferably of the above thickness, onto powdered biocompatible and bioabsorbable substrates; as a nanocryst. coating and converted into a powder; or as a powder of the antimicrobial metal which is cold worked to impart atomic disorder. Methods of preparing the above antimicrobial materials are thus also provided. For example, a bioabsorbable alginate wound dressing (Kaltostat) was coated by nanocryst. silver under sputtering conditions. The silver-coated alginate dressing induced 6.2 log reduction of Pseudomonas aeruginosa in the 2 h test period, thus demonstrating an excellent bacterial killing capacity of the silver-coated alginate dressing.

L8 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:762783 HCAPLUS
DOCUMENT NUMBER: 135:322723
TITLE: Proteins deposited onto sparingly soluble biocompatible particles for controlled protein release into a biological environment from a polymer matrix
INVENTOR(S): Shih, Chung; Zentner, Gaylen; Piao, Ai-Zhi
PATENT ASSIGNEE(S): Macromed, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076558	A1	20011018	WO 2001-US11217	20010406

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002015737	A1	20020207	US 2001-827100	20010405
US 6998137	B2	20060214		
CA 2405030	A1	20011018	CA 2001-2405030	20010406
EP 1267838	A1	20030102	EP 2001-924765	20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010319	A	20030729	BR 2001-10319	20010406
NZ 521994	A	20030829	NZ 2001-521994	20010406
JP 2004507450	T	20040311	JP 2001-574076	20010406
MX 2002PA09790	A	20030619	MX 2002-PA9790	20021004
ZA 2002008039	A	20040204	ZA 2002-8039	20021007
IN 2002MN01387	A	20040904	IN 2002-MN1387	20021007
PRIORITY APPLN. INFO.:			US 2000-195700P P	20000407
			US 2001-827100 A	20010405
			WO 2001-US11217 W	20010406

AB The present invention relates to compns. and methods for the modulated release of one or more proteins or peptides. The composition is comprised of a biocompatible polymeric matrix, a protein and/or peptide, and a sparingly water-soluble or essentially insol. particle. The protein is deposited by adsorption or some other mechanism onto the sparingly water-soluble biocompatible particle wherein the protein-particle combination is dispersed within the polymeric matrix. The deposition of the protein onto the particle acts to modulate the release of the protein or peptide from dosage forms including long-acting dosage systems. To a solution of 5 mg/3mL human growth hormone was added to 100 mg of zinc carbonate and the suspension was allowed to stand in a refrigerator at 4° for 16 h. HPLC anal. showed that the mass balance recovery of hGH, after removal of zinc using EDTA, was quant. In vivo pharmacokinetics of hGH sustained-release formulation was studied in rats.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 35 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2001695543 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11745788
TITLE: Encapsulation and stabilization of nerve growth factor into poly(lactic-co-glycolic) acid microspheres.
AUTHOR: Lam X M; Duenas E T; Cleland J L
CORPORATE SOURCE: Department of Pharmaceutical Research and Development, Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080, USA.. lam.xanthe@gene.com
SOURCE: Journal of pharmaceutical sciences, (2001 Sep) Vol. 90, No. 9, pp. 1356-65.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 18 Dec 2001
Last Updated on STN: 28 Feb 2002
Entered Medline: 27 Feb 2002

AB The development of a stable sustained-release formulation of recombinant human nerve growth factor (rhNGF) for the treatment of neuronal diseases is described. The protein was encapsulated into poly(lactic-co-glycolic) acid (PLGA) microspheres using a spray freeze drying technique. Liquid nitrogen and cold ethanol were used to spray-freeze-dry solid rhNGF that had been suspended in a solution of PLGA dissolved in ethyl acetate. When excipients such as sugar (trehalose), surfactant (pluronic F68), and poly(ethylene glycol) (PEG) were added to the PLGA formulation to protect

rhNGF from degradation during spray freeze drying, the protein degraded via aggregation during in vitro release. The formation of an insoluble rhNGF-zinc complex prior to encapsulation into PLGA microspheres stabilized the protein during both microencapsulation and release. In this study, we have demonstrated that the addition of zinc acetate in a 1:12 rhNGF-to-zinc acetate molar ratio in a solid rhNGF formulation (4 mM sodium bicarbonate at pH 7.4) improves stability of rhNGF during release at 37 degrees C (physiological temperature). The stabilization may be due to rhNGF complexation with zinc to form stable aggregates. The PLGA formulation consisting of 10% rhNGF encapsulated in 12 kDa PLGA (50:50 lactide/glycolide) provided a continuous release of 14 days. The low initial burst (approximately 1%) and controlled-release rate were achieved by the addition of 3 or 6% solid zinc carbonate to the polymer phase during microencapsulation.
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L8 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:494431 HCAPLUS
DOCUMENT NUMBER: 136:42694
TITLE: Controlled release of insulin from injectable biodegradable triblock copolymer
AUTHOR(S): Kim, Young Jin; Choi, Suna; Koh, Jae Joon; Lee, Minhyung; Ko, Kyung Soo; Kim, Sung Wan
CORPORATE SOURCE: Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112-5820, USA
SOURCE: Pharmaceutical Research (2001), 18(4), 548-550
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A water soluble, biodegradable ABA triblock copolymer of poly(DL-lactic acid-co-glycolic acid)-b-ethylene glycol-b-(DL-lactic acid-co-glycolic acid) (ReGel) was used as a drug delivery carrier for continuous release of human insulin. This copolymer is a free flowing sol below 15° in aqueous solns. and forms a high viscosity gel at body temperature The release of human insulin from ReGel exhibited no initial burst and a constant release (zero-order) rate in vitro test due to modification of the association states of insulin by zinc. Animal studies using SD rats were performed to verify, in vivo, the release profile of insulin from ABA block copolymer. ReGel formulation maintained insulin secretion up to 15 days, which could allow diabetic patients to reduce the number of insulin injection twice a month for basal insulin requirements.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:909065 HCAPLUS
DOCUMENT NUMBER: 134:61536
TITLE: Controlled-release of metal cation-stabilized interferon
INVENTOR(S): Tracy, Mark A.; Bernstein, Howard; Khan, M. Amin
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: U.S., 20 pp., Cont.-in-part of U.S. 5,711,968.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6165508	A	20001226	US 1997-765558	19970307

US 5711968	A	19980127	US 1994-279784	19940725
CA 2195994	A1	19960208	CA 1995-2195994	19950607
CN 1154653	A	19970716	CN 1995-194396	19950607
HU 77136	A2	19980302	HU 1997-220	19950607
HU 221602	B	20021128		
US 6514533	B1	20030204	US 1997-934830	19970922
AU 9871908	A	19980813	AU 1998-71908	19980616
AU 706180	B2	19990610		
US 6379701	B1	20020430	US 2000-664299	20000918
US 2003031716	A1	20030213	US 2002-92365	20020306
US 6780434	B2	20040824		

PRIORITY APPLN. INFO.:

US 1994-279784	A2	19940725
US 1992-984323	B2	19921202
US 1995-473544	A2	19950607
US 1995-477725	A2	19950607
US 1995-478502	A2	19950607
US 1995-483318	A2	19950607
WO 1995-US7348	W	19950607
US 1995-521744	B1	19950831
US 1997-765558	A2	19970307
US 2000-664299	A1	20000918

AB This invention relates to a composition, and method of forming said composition, for the controlled-release of interferon. The controlled release composition of this invention comprises a biocompatible polymer and particles of metal cation-stabilized interferon, wherein the particles are dispersed within the biocompatible polymer. The method of the invention, for producing a composition for the controlled release of interferon, includes dissolving a polymer in a polymer solvent to form a polymer solution, dispersing particles of metal cation-stabilized interferon particles in the polymer solution, and then solidifying the polymer to form a polymeric matrix containing a dispersion of the interferon particles. Microspheres of lactide-glycolide block copolymer containing Zn2+-stabilized interferon particles and sodium bicarbonate were prepared, and tested in rats for the in vivo release of IFN-α,2b.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:334526 HCAPLUS

TITLE: Controlled insulin release from biodegradable phase transition polymer.

AUTHOR(S): Kim, Young Jin; Koh, Jae Joon; Kim, Sung Wan

CORPORATE SOURCE: Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112-5820, USA

SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), POLY-346. American Chemical Society: Washington, D. C.
CODEN: 69CLAC

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB For an effective injectable formulation and controlled release of insulin, a water soluble, a biodegradable triblock copolymer of poly((DL-lactide-co-glycolide)-b-ethylene glycol-b-(DL-lactide-co-glycolide)) (1500-1000-1500) was used in this study. The aqueous solution of the triblock copolymer at a concentration of 23 wt% showed a sol-to-gel transition around 15°C as increasing temperature The mixture of insulin and the polymer in cold phosphate buffered saline (PBS, pH 7.4, ionic strength 10 mM) was gelatinized by expositing the solution to 37°C. The insulin loading content was 5.04

mg/mL and zinc content varied because zinc content in insulin modifies the insulin association ranging from monomer to hexamer. The insulin release in PBS at 37°C was monitored by the reversed-phase high performance liquid chromatog.(RP-HPLC) and the release profile was controlled by the zinc content. Almost linear release profile over 10 days was obtained at a zinc concentration of 0.2 wt% of insulin. Animal study using a diabetic rat model is under investigation.

L8 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:539320 HCAPLUS
DOCUMENT NUMBER: 127:210362
TITLE: Modulated release from biocompatible polymers
INVENTOR(S): Bernstein, Howard; Zhang, Yan; Khan, M. Amin; Tracy, Mark A.
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 849,754, abandoned
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5656297	A	19970812	US 1994-237057	19940503
AT 154240	T	19970615	AT 1993-907490	19930312
US 5413797	A	19950509	US 1994-268715	19940630
CA 2189254	A1	19951109	CA 1995-2189254	19950503
CA 2189254	C	20061010		
WO 9529664	A1	19951109	WO 1995-US5511	19950503
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9524674	A	19951129	AU 1995-24674	19950503
AU 688506	B2	19980312		
EP 758227	A1	19970219	EP 1995-918942	19950503
EP 758227	B1	20040114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504017	T	19980414	JP 1995-528506	19950503
AT 257696	T	20040115	AT 1995-918942	19950503
US 5912015	A	19990615	US 1998-56566	19980407
AU 9871878	A	19980730	AU 1998-71878	19980611
AU 704647	B2	19990429		
US 6368630	B1	20020409	US 1999-274613	19990323
US 2002168410	A1	20021114	US 2002-39285	20020103
US 6749866	B2	20040615		
US 2004241230	A1	20041202	US 2004-797718	20040310

PRIORITY APPLN. INFO.:

US 1992-849754	B2	19920312
US 1994-237057	A	19940503
WO 1995-US5511	W	19950503
US 1996-727531	A1	19961022
US 1998-56566	A1	19980407
US 1999-274613	A1	19990323
US 2002-39285	A1	20020103

AB The present invention relates to a composition for the modulated release of a biol. active agent. The composition comprises a biocompatible polymeric matrix, a biol. active agent which is dispersed within the polymeric matrix, and a

metal cation component which is sep. dispersed within the polymeric matrix, whereby the metal cation component modulates the release of the biol. active agent from the polymeric matrix. The present invention also relates to a method for modulating the release of a biol. active agent from a biocompatible polymeric matrix, comprising the steps of dissolving a biocompatible polymer in a solvent to form a polymer solution and also sep. dispersing a metal cation component and a biol. active agent within the polymer solution The polymer solution is then solidified to form a polymeric matrix, wherein at least a significant portion of the metal cation component is dispersed in the polymeric matrix sep. from the biol. active protein, and whereby the metal cation component modulates the release of the biol. active agent from the polymeric matrix. Lactide-glycolide polymer matrixes containing $MgCO_3$, $Mg(OH)_2$ and $ZnCO_3$ were prepared

L8 ANSWER 32 OF 35 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:496139 SCISEARCH
THE GENUINE ARTICLE: XH041
TITLE: The stabilization and encapsulation of human growth hormone into biodegradable microspheres
AUTHOR: Johnson O L (Reprint); Jaworowicz W; Cleland J L; Bailey L; Charnis M; Duenas E; Wu C C; Shepard D; Magil S; Last T; Jones A J S; Putney S D
CORPORATE SOURCE: ALKERMES INC, CAMBRIDGE, MA 02139; GENENTECH INC, S SAN FRANCISCO, CA 94080
COUNTRY OF AUTHOR: USA
SOURCE: PHARMACEUTICAL RESEARCH, (JUN 1997) Vol. 14, No. 6, pp. 730-735.
ISSN: 0724-8741.
PUBLISHER: PLENUM PUBL CORP, 233 SPRING ST, NEW YORK, NY 10013.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 32
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose. To produce and evaluate sustained-acting formulations of recombinant human growth hormone (rhGH) made by a novel microencapsulation process.

Methods. The protein was stabilized by forming an insoluble complex with zinc and encapsulated into microspheres of poly (D,L-lactide co-glycolide) (PLGA) which differed in polymer molecular weight (8-31kD), polymer end group, and zinc content. The encapsulation procedure was cryogenic, non-aqueous, and did not utilize surfactants or emulsification. The rhGH extracted from each of these microsphere formulations was analyzed by size-exclusion, ion-exchange and reversed-phase chromatography, SDS-polyacrylamide gel electrophoresis, peptide mapping, and cell proliferation of a cell line expressing the hGH receptor. In addition, the in vivo release profile was determined after subcutaneous administration of the microspheres to rats and juvenile rhesus monkeys.

Results. Protein and bioactivity analyses of the rhGH extracted from three different microsphere formulations showed that the encapsulated protein was unaltered relative to the protein before encapsulation. In vivo, microsphere administration to rats or monkeys induced elevated levels of serum rhGH for up to one month, more than 20-fold longer than was induced by the same amount of protein injected subcutaneously as a solution. The rate of protein release differed between the three microsphere formulations and was determined by the molecular weight and hydrophobicity of the PLGA. The serum rhGH profile, after three

sequential monthly doses of the one formulation examined, was reproducible and showed no dose accumulation.

Conclusions. Using a novel process, rhGH can be stabilized and encapsulated in a solid state into PLGA microspheres and released with unaltered properties at different rates.

L8 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:336393 HCAPLUS
DOCUMENT NUMBER: 125:19009
TITLE: Solid delivery systems for controlled release of molecules incorporated therein
INVENTOR(S): Roser, Bruce Joseph; Colaco, Camilo; Jerrow, Mohamed Abdel Zahra; Blair, Julian Alexander; Kampinga, Jaap; Wardell, James Lewis; Duffy, John Alistair
PATENT ASSIGNEE(S): Quadrant Holdings Cambridge Limited, UK
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603978	A1	19960215	WO 1995-GB1861	19950804
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6290991	B1	20010918	US 1994-349029	19941202
CA 2197982	A1	19960215	CA 1995-2197982	19950804
AU 9531851	A	19960304	AU 1995-31851	19950804
AU 688557	B2	19980312		
EP 773781	A1	19970521	EP 1995-927856	19950804
EP 773781	B1	20031022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10503769	T	19980407	JP 1995-506345	19950804
HU 77777	A2	19980828	HU 1998-694	19950804
CN 1204959	A	19990113	CN 1995-195496	19950804
EP 1138319	A2	20011004	EP 2001-116637	19950804
EP 1138319	A3	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
EP 1138337	A2	20011004	EP 2001-116638	19950804
EP 1138337	A3	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
RU 2177785	C2	20020110	RU 1997-103529	19950804
EE 3593	B1	20020215	EE 1997-62	19950804
PL 184068	B1	20020830	PL 1995-318898	19950804
SK 283026	B6	20030204	SK 1997-277	19950804
AT 252373	T	20031115	AT 1995-927856	19950804
PT 773781	T	20040331	PT 1995-927856	19950804
ES 2208687	T3	20040616	ES 1995-927856	19950804
EP 1516615	A2	20050323	EP 2004-29125	19950804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
CZ 297431	B6	20061213	CZ 1997-476	19950804
RO 121407	B1	20070530	RO 1997-293	19970213
FI 9700867	A	19970408	FI 1997-867	19970228
NO 9701688	A	19970411	NO 1997-1688	19970411
AU 9871864	A	19980820	AU 1998-71864	19980612

AU 707605	B2	19990715			
US 6331310	B1	20011218	US 2000-628380		20000801
US 2001038858	A1	20011108	US 2001-755737		20010105
US 6586006	B2	20030701			
US 2002012687	A1	20020131	US 2001-945180		20010831
US 6565871	B2	20030520			
US 2003054040	A1	20030320	US 2002-280468		20021025
US 6811792	B2	20041102			
US 2003147961	A1	20030807	US 2003-376136		20030227
US 6893657	B2	20050517			
US 2004052825	A1	20040318	US 2003-652212		20030829
US 7056495	B2	20060606			
US 2004219206	A1	20041104	US 2004-857100		20040528
US 2005276845	A1	20051215	US 2005-134573		20050520
US 2005276846	A1	20051215	US 2005-134700		20050520
US 2005276759	A1	20051215	US 2005-134701		20050520
JP 2006056898	A	20060302	JP 2005-284596		20050929
PRIORITY APPLN. INFO.:			GB 1994-15810	A	19940804
			US 1994-349029	A	19941202
			EP 1995-927856	A3	19950804
			JP 1996-506345	A3	19950804
			WO 1995-GB1861	W	19950804
			US 1997-500877	B1	19970818
			US 2000-628380	A1	20000801
			EP 2001-116638	A3	20010713
			US 2001-945180	A1	20010831
			US 2003-376136	A1	20030227
			US 2003-652212	A1	20030829

AB Solid dosage delivery systems suitable for delivery of bioactive materials s.c., intradermal, i.m., and i.v. are disclosed. The delivery systems comprise a vitreous vehicle, e.g. polyol, loaded with the guest substance and capable of releasing the guest substance in situ at various controlled rates. Microparticles were prepared by spray drying a solution of 0.39 M trehalose, 0.14 M calcium lactate and 0.5% MB9. This particles were coated by addition of a saturated solution of zinc palmitate in toluene and cooling at 60-30°. The particles were then filtered under vacuum to remove excess zinc palmitate, washed with acetone, and air-dried. The resulting powder remained unwetted in water for ≥ 3 days and released MB9 slowly into the water.

L8 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:311458 HCAPLUS
DOCUMENT NUMBER: 124:325425
TITLE: Controlled release of metal cation-stabilized interferon
INVENTOR(S): Tracy, Mark A.; Bernstein, Howard; Khan, M. Amin
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603116	A1	19960208	WO 1995-US7348	19950607

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5711968	A	19980127	US 1994-279784	19940725
CA 2195994	A1	19960208	CA 1995-2195994	19950607
AU 9528222	A	19960222	AU 1995-28222	19950607
AU 691631	B2	19980521		
EP 772435	A1	19970514	EP 1995-923783	19950607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1154653	A	19970716	CN 1995-194396	19950607
HU 77136	A2	19980302	HU 1997-220	19950607
HU 221602	B	20021128		
JP 10503198	T	19980324	JP 1995-505727	19950607
US 6514533	B1	20030204	US 1997-934830	19970922
AU 9871908	A	19980813	AU 1998-71908	19980616
AU 706180	B2	19990610		
US 6379701	B1	20020430	US 2000-664299	20000918
US 2003031716	A1	20030213	US 2002-92365	20020306
US 6780434	B2	20040824		

PRIORITY APPLN. INFO.:

US 1994-279784	A	19940725
US 1992-984323	B2	19921202
US 1995-473544	A2	19950607
US 1995-477725	A2	19950607
US 1995-478502	A2	19950607
US 1995-483318	A2	19950607
WO 1995-US7348	W	19950607
US 1995-521744	B1	19950831
US 1997-765558	A2	19970307
US 2000-664299	A1	20000918

AB A controlled-release interferon (I) composition comprises a biocompatible polymer and particles of metal cation-stabilized I, wherein the particles are dispersed within the biocompatible polymer. The method includes dissolving the polymer in a solvent to form a polymer solution, dispersing particles of metal cation-stabilized interferon particles in the polymer solution, and then solidifying the polymer to form a polymeric matrix containing a dispersion of the interferon particles. A 10 mM Zn+2 solution was prepared from deionized water and zinc acetate dihydrate and then was added to the I-α2b solution to form Zn+2-I-α2b solution with a final I-α2b concentration of 1.3 mg/mL and Zn+2:I-α2b molar ratio of 2:1, 4:1, or 10:1, resp. and pH was adjusted to 7.1 by adding 1% acetic acid. The suspension of Zn+2-stabilized I-α2b was micronized by ultrasonic and lyophilized.

L8 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:38799 HCAPLUS
DOCUMENT NUMBER: 124:66652
TITLE: Modulated-release pharmaceuticals containing a biocompatible polymer matrix and a metal cation
INVENTOR(S): Bernstein, Howard; Zhang, Yan; Khan, M. Amin; Tracy, Mark A.
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9529664	A1	19951109	WO 1995-US5511	19950503
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,				

TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5656297	A	19970812	US 1994-237057	19940503
CA 2189254	A1	19951109	CA 1995-2189254	19950503
CA 2189254	C	20061010		
AU 9524674	A	19951129	AU 1995-24674	19950503
AU 688506	B2	19980312		
EP 758227	A1	19970219	EP 1995-918942	19950503
EP 758227	B1	20040114		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 10504017	T	19980414	JP 1995-528506	19950503
AT 257696	T	20040115	AT 1995-918942	19950503
US 5912015	A	19990615	US 1998-56566	19980407
US 6368630	B1	20020409	US 1999-274613	19990323
US 2002168410	A1	20021114	US 2002-39285	20020103
US 6749866	B2	20040615		
US 2004241230	A1	20041202	US 2004-797718	20040310

PRIORITY APPLN. INFO.:

US 1994-237057	A2	19940503
US 1992-849754	B2	19920312
WO 1995-US5511	W	19950503
US 1996-727531	A1	19961022
US 1998-56566	A1	19980407
US 1999-274613	A1	19990323
US 2002-39285	A1	20020103

AB A composition for the modulated release of a biol. active agent comprises a biocompatible polymeric matrix, a biol. active agent which is dispersed within the polymeric matrix, and a metal cation component which is sep. dispersed within the polymeric matrix, whereby the metal cation component modulates the release of the biol. active agent from the polymeric matrix. A 10 mM solution of zinc acetate dihydrate was added to interferon-α 2, b (I) to obtain a final concentration of 1.3 mg/mL I, then the pH was adjusted to 7.1 with acetic acid. The above stabilized Zn-I suspension was micronized, frozen, and lyophilized to obtain I powder. Zinc carbonate and I powder were added in different proportions to a solution of 0.4g poly(lactide-glycolide) (II) in 4mL methylene chloride and then were microencapsulated in II to form I microspheres. Microsphere doses of 0.9 mg/kg were injected into the intrascapular region of the rats and blood concentration of I was measured at different times. The sustained-release level of immunol. active I was modulated depending upon the ratio of zinc carbonate to Zn-I in the microspheres, the higher the ratio of zinc carbonate demonstrated lower release rates of I from the microspheres.

=> d his

(FILE 'HOME' ENTERED AT 13:33:08 ON 18 OCT 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007

L1	153512	S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2	55988	S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3	423	S L1 AND L2
L4	1137	S POLYLACTIDE(3W)GLYCOLIDE?
L5	2	S L3 AND L4
L6	220	S L1 AND GLYCOLID?
L7	40	S L2 AND L6
L8	35	DUP REM L7 (5 DUPLICATES REMOVED)

```
=> e bernstein h/au
E1            7      BERNSTEIN GUSTAVE/AU
E2            1      BERNSTEIN GUY T/AU
E3          772 --> BERNSTEIN H/AU
E4            6      BERNSTEIN H A/AU
E5           43      BERNSTEIN H B/AU
E6            4      BERNSTEIN H C/AU
E7          139      BERNSTEIN H D/AU
E8            5      BERNSTEIN H E/AU
E9            3      BERNSTEIN H F/AU
E10         691      BERNSTEIN H G/AU
E11         186      BERNSTEIN H H/AU
E12           4      BERNSTEIN H I/AU

=> s e3
L9          772 "BERNSTEIN H"/AU

=> e zhang y/au
E1            1      ZHANG XZH/AU
E2            1      ZHANG XZHENGCHENG/AU
E3        29875 --> ZHANG Y/AU
E4            2      ZHANG Y */AU
E5          227      ZHANG Y A/AU
E6           13      ZHANG Y ALEX/AU
E7          637      ZHANG Y B/AU
E8            1      ZHANG Y B B/AU
E9            1      ZHANG Y BING/AU
E10        1079      ZHANG Y C/AU
E11           1      ZHANG Y C Q/AU
E12          59      ZHANG Y CLARE/AU

=> s e3
L10       29875 "ZHANG Y"/AU

=> e khan m a/au
E1           12      KHAN LYLA R/AU
E2         2620      KHAN M/AU
E3         7371 --> KHAN M A/AU
E4            2      KHAN M A */AU
E5          121      KHAN M A A/AU
E6            2      KHAN M A AARIFF/AU
E7            6      KHAN M A ALI/AU
E8            6      KHAN M A AZIZ/AU
E9            8      KHAN M A B/AU
E10           5      KHAN M A G/AU
E11           2      KHAN M A GHAFFAR/AU
E12          53      KHAN M A H/AU

=> s e3
L11        7371 "KHAN M A"/AU

=> e tracy m a/au
E1            2      TRACY LYNDON S/AU
E2          307      TRACY M/AU
E3           52 --> TRACY M A/AU
E4           33      TRACY M B/AU
E5           14      TRACY M C/AU
E6            9      TRACY M D/AU
E7           15      TRACY M E/AU
E8           37      TRACY M F/AU
E9            1      TRACY M G/AU
E10          11      TRACY M J/AU
E11           1      TRACY M J H/AU
E12           1      TRACY M JAMES/AU
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=> s e3
L12          52 "TRACY M A"/AU

=> d his

     (FILE 'HOME' ENTERED AT 13:33:08 ON 18 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
L1        153512 S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2         55988 S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3           423 S L1 AND L2
L4          1137 S POLYLACTIDE(3W)GLYCOLIDE?
L5             2 S L3 AND L4
L6           220 S L1 AND GLYCOLID?
L7            40 S L2 AND L6
L8            35 DUP REM L7 (5 DUPLICATES REMOVED)
                 E BERNSTEIN H/AU
L9           772 S E3
                 E ZHANG Y/AU
L10        29875 S E3
                 E KHAN M A/AU
L11         7371 S E3
                 E TRACY M A/AU
L12           52 S E3

=> s l9 or l10 or l11 or l12
L13        38042 L9 OR L10 OR L11 OR L12

=> s l6 and l13
L14           11 L6 AND L13

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15            5 DUP REM L14 (6 DUPLICATES REMOVED)

=> d l-5 ibib ab

L15 ANSWER 1 OF 5     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2001232526     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11205730
TITLE:              Protein spray-freeze drying. Effect of atomization
                    conditions on particle size and stability.
AUTHOR:             Costantino H R; Firouzabadian L; Hogeland K; Wu C; Beganski
                    C; Carrasquillo K G; Cordova M; Griebenow K; Zale S E;
                    Tracy M A
CORPORATE SOURCE:   Alkermes, Inc., Cambridge, MA 02139, USA..
                    rick.costantino@alkermes.com
CONTRACT NUMBER:    S06 GM8102-26S1 (NIGMS)
SOURCE:             Pharmaceutical research, (2000 Nov) Vol. 17, No. 11, pp.
                    1374-83.
                    Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200105
ENTRY DATE:         Entered STN: 17 May 2001
                    Last Updated on STN: 17 May 2001
                    Entered Medline: 3 May 2001
AB   PURPOSE: To investigate the effect of atomization conditions on
```

particle size and stability of spray-freeze dried protein. METHODS: Atomization variables were explored for excipient-free (no zinc added) and zinc-complexed bovine serum albumin (BSA). Particle size was measured by laser diffraction light scattering following sonication in organic solvent containing poly(lactide-co-glycolide) (PLG). Powder surface area was determined from the N2 vapor sorption isotherm. Size-exclusion chromatography (SEC) was used to assess decrease in percent protein monomer. Fourier-transform infrared (FTIR) spectroscopy was employed to estimate protein secondary structure. PLG microspheres were made using a non-aqueous, cryogenic process and release of spray-freeze dried BSA was assessed in vitro. RESULTS: The most significant atomization parameter affecting particle size was the mass flow ratio (mass of atomization N2 relative to that for liquid feed). Particle size was inversely related to specific surface area and the amount of protein aggregates formed. Zinc-complexation reduced the specific surface area and stabilized the protein against aggregation. FTIR data indicated perturbations in secondary structure upon spray-freeze drying for both excipient-free and zinc-complexed protein. CONCLUSIONS: Upon sonication, spray-freeze dried protein powders exhibited friability, or susceptibility towards disintegration. For excipient-free protein, conditions where the mass flow ratio was > -0.3 yielded sub-micron powders with relatively large specific surface areas. Reduced particle size was also linked to a decrease in the percentage of protein monomer upon drying. This effect was ameliorated by zinc -complexation, via a mechanism involving reduction in specific surface area of the powder rather than stabilization of secondary structure. Reduction of protein particle size was beneficial in reducing the initial release (burst) of the protein encapsulated in PLG microspheres.

L15 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:672407 HCAPLUS
DOCUMENT NUMBER: 134:168252
TITLE: Spray-freeze drying to produce protein particles for encapsulation in polymer delivery systems
AUTHOR(S): Costantino, H. R.; Firouzabadian, L.; Hogeland, K.; Wu, C. -C.; Beganski, C.; Zale, S. E.; Tracy, M. A.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 974-975
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increasing the atomization mass flow ratio results in a finer, more friable structure for spray-freeze dried protein powder. This allow for reduction of particle size on dispersion in organic solvent containing PLG and subsequent microencapsulation. As expected, the reduction in the size of the encapsulated particles translated into a significant reduction in the amount of material available for initial release.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999305151 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10378806
TITLE: Factors affecting the degradation rate of poly(lactide-co-glycolide) microspheres in vivo and in vitro.
AUTHOR: Tracy M A; Ward K L; Firouzabadian L; Wang Y; Dong N; Qian R; Zhang Y

CORPORATE SOURCE: Alkermes Inc., Cambridge, MA 02139, USA..
mark_tracy@alkermes.com
SOURCE: Biomaterials, (1999 Jun) Vol. 20, No. 11, pp. 1057-62.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
(IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 16 Aug 1999

AB The purpose of this work was to study the degradation of poly(lactide-co-glycolide) (PLG) microspheres in vivo and in vitro. Degradation rate constants were determined by measuring the polymer molecular weight as a function of time by gel-permeation chromatography. The effects of PLG chemistry and the effects of encapsulating the sparingly soluble salt zinc carbonate and the protein recombinant human growth hormone (rhGH) on the degradation rate were assessed. It was found that in vivo degradation was faster than in vitro degradation. In addition, different types of PLGs were found to degrade at different rates depending on the chemistry of the polymer end group and, to a lesser extent, the molecular weight. Finally, zinc carbonate was found to retard the degradation of some PLGs. These degradation studies have proved valuable in the design of sustained release microsphere products.

L15 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:481734 HCAPLUS
DOCUMENT NUMBER: 129:235498
TITLE: Factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro
AUTHOR(S): Tracy, M. A.; Ward, K. L.; Firouzabadian, L.; Wang, Y.; Dong, N.; Qian, R.; Zhang, Y.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 148-149
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PLG microsphere degradation was studied in vivo and in vitro. Degradation was faster in vivo than in vitro. In addition, different types of PLG's degraded at very different rates depending on the chemical of the polymer end group and, to a lesser extent, the mol. weight The sparingly soluble salt, Zn carbonate, also retarded degradation of capped PLG's. The addition of protein did not affect degradation

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:463753 HCAPLUS
DOCUMENT NUMBER: 127:113254
TITLE: In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres
AUTHOR(S): Tracy, M. A.; Zhang, Y.; Verdon, S. L.; Dong, N.; Riley, M. G. I.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA

SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 623-624
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The degradation of poly(lactide-co-glycolide) microspheres was faster in-vivo than in-vitro. The PLG end group had the greatest effect on degradation, with the uncapped PLG degrading faster than the capped compds.

=> s (zinc (w)(carbonat? or acetat? or chlorid? or sulfate? or citrate?)) and l15
L16 3 (ZINC (W)(CARBONAT? OR ACETAT? OR CHLORID? OR SULFATE? OR CITRAT E?)) AND L15

=> d 1-3 ibib ab

L16 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 1999305151 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10378806
TITLE: Factors affecting the degradation rate of poly(lactide-co-glycolide) microspheres in vivo and in vitro.
AUTHOR: Tracy M A; Ward K L; Firouzabadian L; Wang Y; Dong N; Qian R; Zhang Y
CORPORATE SOURCE: Alkermes Inc., Cambridge, MA 02139, USA..
mark_tracy@alkermes.com
SOURCE: Biomaterials, (1999 Jun) Vol. 20, No. 11, pp. 1057-62.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
(IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 16 Aug 1999
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L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:481734 HCAPLUS
DOCUMENT NUMBER: 129:235498
TITLE: Factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro
AUTHOR(S): Tracy, M. A.; Ward, K. L.; Firouzabadian, L.; Wang, Y.; Dong, N.; Qian, R.; Zhang, Y.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA

SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 148-149
CODEN: PCRMEY; ISSN: 1022-0178
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REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:463753 HCAPLUS
DOCUMENT NUMBER: 127:113254
TITLE: In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres
AUTHOR(S): Tracy, M. A.; Zhang, Y.; Verdon, S. L.; Dong, N.; Riley, M. G. I.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 623-624
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The degradation of poly(lactide-co-glycolide) microspheres was faster in-vivo than in-vitro. The PLG end group had the greatest effect on degradation, with the uncapped PLG degrading faster than the capped compds.

=> d 1-3 kwic

L16 ANSWER 1 OF 3 MEDLINE on STN
TI Factors affecting the degradation rate of poly(lactide-co-glycolide) microspheres in vivo and in vitro.
AU Tracy M A; Ward K L; Firouzabadian L; Wang Y; Dong N; Qian R; Zhang Y
AB The purpose of this work was to study the degradation of poly(lactide-co-glycolide) (PLG) microspheres in vivo and in vitro. Degradation rate constants were determined by measuring the polymer molecular weight as a function of time by gel-permeation chromatography. The effects of PLG chemistry and the effects of encapsulating the sparingly soluble salt zinc carbonate and the protein recombinant human growth hormone (rhGH) on the degradation rate were assessed. It was found that in vivo. . . . degradation. In addition, different types of PLGs were found to degrade at different rates depending on the chemistry of the polymer end group and, to a lesser extent, the molecular weight. Finally, zinc carbonate was found to retard the degradation of some PLGs. These degradation studies have proved valuable in the design of sustained. . .
CT . . .
chemistry
Lactic Acid: ME, metabolism
Materials Testing
Microspheres
Molecular Weight
*Polyglycolic Acid

Polyglycolic Acid: CH, chemistry
Polyglycolic Acid: ME, metabolism
*Polymers
Polymers: CH, chemistry
Polymers: ME, metabolism
Rats
Rats, Sprague-Dawley
Zinc Compounds: PD, pharmacology

RN 26009-03-0 (Polyglycolic Acid); 3486-35-9 (zinc carbonate); 50-21-5 (Lactic Acid)

CN 0 (Biocompatible Materials); 0 (Carbonates); 0 (Drug Carriers); 0 (Polymers); 0 (Zinc Compounds); 0 (polylactic acid-polyglycolic acid copolymer)

L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro

AU Tracy, M. A.; Ward, K. L.; Firouzabadian, L.; Wang, Y.; Dong, N.; Qian, R.; Zhang, Y.

AB . . . than in vitro. In addition, different types of PLG's degraded at very different rates depending on the chemical of the polymer end group and, to a lesser extent, the mol. weight The sparingly soluble salt, Zn carbonate, also retarded degradation of. . .

ST glycolide lactide microsphere degrdn

IT Polyesters, biological studies
RL: PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(dilactone-based; factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

IT Polymer degradation kinetics
(factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

IT Proteins, general, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

IT Drug delivery systems
(microspheres; factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

IT 26780-50-7, Glycolide-lactide copolymer
RL: PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

IT 3486-35-9, Zinc carbonate 12629-01-5, Human growth hormone
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro)

L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

TI In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres

AU Tracy, M. A.; Zhang, Y.; Verdon, S. L.; Dong, N.; Riley, M. G. I.

AB The degradation of poly(lactide-co-glycolide) microspheres was faster in-vivo than in-vitro. The PLG end group had the greatest effect on degradation, with the uncapped PLG. . .

IT Polymer degradation
(biol.; degradation of poly(lactide-co-glycolide) microspheres)

IT Polymer degradation
(degradation of poly(lactide-co-glycolide) microspheres)

```
IT   Polyesters, biological studies
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (dilactone-based, end-capped; degradation of poly(lactide-co-
        glycolide) microspheres)
IT   Drug delivery systems
        (microspheres; degradation of poly(lactide-co-glycolide)
        microspheres)
IT   3486-35-9, Zinc carbonate
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (degradation of poly(lactide-co-glycolide) microspheres)
IT   26780-50-7, Glycolide-lactide copolymer
     RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (end-capped; degradation of poly(lactide-co-glycolide)
        microspheres)


=> d his

     (FILE 'HOME' ENTERED AT 13:33:08 ON 18 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
L1        153512 S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2         55988 S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3           423 S L1 AND L2
L4          1137 S POLYLACTIDE(3W)GLYCOLIDE?
L5             2 S L3 AND L4
L6           220 S L1 AND GLYCOLID?
L7            40 S L2 AND L6
L8            35 DUP REM L7 (5 DUPLICATES REMOVED)
                 E BERNSTEIN H/AU
L9           772 S E3
                 E ZHANG Y/AU
L10        29875 S E3
                 E KHAN M A/AU
L11         7371 S E3
                 E TRACY M A/AU
L12           52 S E3
L13        38042 S L9 OR L10 OR L11 OR L12
L14           11 S L6 AND L13
L15            5 DUP REM L14 (6 DUPLICATES REMOVED)
L16            3 S (ZINC (W)(CARBONAT? OR ACETAT? OR CHLORID? OR SULFATE? OR CIT

=> d 1-3 ibib ab

L16  ANSWER 1 OF 3     MEDLINE on STN
ACCESSION NUMBER:    1999305151      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 10378806
TITLE:               Factors affecting the degradation rate of poly(lactide-co-
                     glycolide) microspheres in vivo and in vitro.
AUTHOR:              Tracy M A; Ward K L; Firouzabadian L; Wang Y;
                     Dong N; Qian R; Zhang Y
CORPORATE SOURCE:    Alkermes Inc., Cambridge, MA 02139, USA..
                     mark_tracy@alkermes.com
SOURCE:              Biomaterials, (1999 Jun) Vol. 20, No. 11, pp. 1057-62.
                     Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       (COMPARATIVE STUDY)
                     (IN VITRO)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
```

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 16 Aug 1999

AB The purpose of this work was to study the degradation of poly(lactide-co-glycolide) (PLG) microspheres in vivo and in vitro. Degradation rate constants were determined by measuring the polymer molecular weight as a function of time by gel-permeation chromatography. The effects of PLG chemistry and the effects of encapsulating the sparingly soluble salt zinc carbonate and the protein recombinant human growth hormone (rhGH) on the degradation rate were assessed. It was found that in vivo degradation was faster than in vitro degradation. In addition, different types of PLGs were found to degrade at different rates depending on the chemistry of the polymer end group and, to a lesser extent, the molecular weight. Finally, zinc carbonate was found to retard the degradation of some PLGs. These degradation studies have proved valuable in the design of sustained release microsphere products.

L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:481734 HCAPLUS
DOCUMENT NUMBER: 129:235498
TITLE: Factors affecting degradation rates of poly(lactide-co-glycolide) microspheres in vivo and in vitro
AUTHOR(S): Tracy, M. A.; Ward, K. L.; Firouzabadian, L.; Wang, Y.; Dong, N.; Qian, R.; Zhang, Y.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 148-149
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PLG microsphere degradation was studied in vivo and in vitro. Degradation was faster in vivo than in vitro. In addition, different types of PLG's degraded at very different rates depending on the chemical of the polymer end group and, to a lesser extent, the mol. weight The sparingly soluble salt, Zn carbonate, also retarded degradation of capped PLG's. The addition of protein did not affect degradation

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:463753 HCAPLUS
DOCUMENT NUMBER: 127:113254
TITLE: In-vivo and in-vitro degradation of poly(lactide-co-glycolide) microspheres
AUTHOR(S): Tracy, M. A.; Zhang, Y.; Verdon, S. L.; Dong, N.; Riley, M. G. I.
CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 623-624
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The degradation of poly(lactide-co-glycolide) microspheres was faster in-vivo than in-vitro. The PLG end group had the greatest effect

on degradation, with the uncapped PLG degrading faster than the capped compds.

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=> d his

     (FILE 'HOME' ENTERED AT 13:33:08 ON 18 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 13:33:39 ON 18 OCT 2007
L1        153512 S (POLYMER? OR MATRIX OR GEL OR PELLET? OR PARTICLE?) AND ZINC
L2         55988 S (CONTROLLED OR MODULAT?)(W)RELEASE?
L3           423 S L1 AND L2
L4          1137 S POLYLACTIDE(3W)GLYCOLIDE?
L5             2 S L3 AND L4
L6           220 S L1 AND GLYCOLID?
L7            40 S L2 AND L6
L8            35 DUP REM L7 (5 DUPLICATES REMOVED)
                 E BERNSTEIN H/AU
L9           772 S E3
                 E ZHANG Y/AU
L10        29875 S E3
                 E KHAN M A/AU
L11         7371 S E3
                 E TRACY M A/AU
L12           52 S E3
L13        38042 S L9 OR L10 OR L11 OR L12
L14           11 S L6 AND L13
L15            5 DUP REM L14 (6 DUPLICATES REMOVED)
L16            3 S (ZINC (W)(CARBONAT? OR ACETAT? OR CHLORID? OR SULFATE? OR CIT
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	Document ID	Kind Codes	Source	Issue Date	Pages
1	US 20060079740 A1		US-PGPUB	20060413	82
2	US 20040241230 A1		US-PGPUB	20041202	26
3	US 20040176672 A1		US-PGPUB	20040909	50
4	US 20040071715 A1		US-PGPUB	20040415	21
5	US 20030114735 A1		US-PGPUB	20030619	38
6	US 20020168410 A1		US-PGPUB	20021114	26
7	US 7181261 B2		USPAT	20070220	53
8	US 7006858 B2		USPAT	20060228	41
9	US 6749866 B2		USPAT	20040615	26

	Title
1	Sensors for detecting substances indicative of stroke, ischemia, or myocardial infarction
2	Modulated release from biocompatible polymers
3	Implantable, retrievable, thrombus minimizing sensors
4	Polymer compositions that stabilize and control the release of formaldehyde-treated vaccine antigens
5	Implantable, retrievable sensors and immunosensors
6	Modulated release from biocompatible polymers
7	Implantable, retrievable, thrombus minimizing sensors
8	Implantable, retrievable sensors and immunosensors
9	Modulated release from biocompatible polymers

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6	US 6749866 B2		USPAT	20040615	26
7	US 6468961 B1		USPAT	20021022	27
8	US 6130200 A		USPAT	20001010	24

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1	Sensors for detecting substances indicative of stroke, ischemia, or myocardial infarction
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4	Modulated release from biocompatible polymers
5	Implantable, retrievable, thrombus minimizing sensors
6	Modulated release from biocompatible polymers
7	Gel composition and methods
8	Gel composition and methods

	L #	Hits	Search Text
1	L1	1672591	polymer or matrix or gel or particle$2 or pellet?
2	L2	2171996	zinc (w)(acetate$2 or carbonat$3 or chlorid$3 or sulfat$3 or citrat$2)
3	L3	494215	l1 same l2
4	L4	67679	(controlled or modulated or slow)adj release$2
5	L5	44659	zinc adj(acetate$2 or carbonat$3 or chlorid$3 or sulfat$3 or citrat$2)
6	L6	8105	l1 same l5
7	L7	31	l4 same l6
8	L8	14642	glycolid$3
9	L9	9	l7 same l8
10	L10	110478	BERNSTEIN ZHANG KHAN TRACY
11	L11	2908	l8 and l10
12	L12	8	l7 and l10